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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,018	09/20/2001	John G Cumming	P 0282964	4357

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EXAMINER

RAO, DEEPAK R

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 09/24/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/937,018

Applicant(s)
Cumming

Examiner
Deepak Rao

Art Unit
1624



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jun 30, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 12, and 13 ☒ are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 9, 10, 12, and 13 ☒ are rejected.
- 7) ☒ Claim(s) 2-8 ☒ are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

This office action is in response to the amendment filed on June 30, 2003.

Claims 1-10 and 12-13 are pending in this application.

The following rejections are withdrawn:

The rejection under 35 U.S.C. 112, second paragraph of the previous office action is hereby withdrawn in view of the amendments.

The rejection under 35 U.S.C. 103(a) over Thompson et al. (J. Med. Chem. 1995) of the previous office action is hereby withdrawn in view of the amendments.

The following rejections are maintained:

1. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Thompson et al. (J. Med. Chem. 1995), for the reasons provided in the previous office action which are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that the specification provides that inhibition of cytokines treats cachexia associated with cancer and not the cancer itself. However, the instant claim is drawn to 'a method of treating a disease or medical condition mediated by cytokines....' and therefore, includes any disease mediated by cytokines. It is well known in the art that 'cytokines' are messenger proteins that allow communication between cells. Nearly every type of disease has a

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cytokine component and further, cytokines contribute to chemical signaling language that controls tissue repair. (As per Encyclopedia of Life Sciences http://www.els.net/els/public/search/search_public.asp keyword 'cytokines'). Therefore, the instant claim includes diseases mediated by intercellular communication. The reference clearly teaches the use of the compounds in the treatment of various diseases mediated by EGFR which is a growth factor receptor, which mediates intercellular communication and thus, teaches the instantly claimed therapeutic method.

2. Claims 1, 9-10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugarkar et al., WO 96/40706, for the reasons provided in the previous office action which are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that person of ordinary skill in the art would not be motivated to select the instantly claimed compounds from the broad genus of the reference. This is not found to be persuasive because the reference clearly teaches bicyclic pyrimidinyl compounds having an anilino group attached to the 4-position, see formula 1 in page 9. Further, the reference discloses a species falling within the genus which is structurally analogous to the instantly claimed genus, see compound #129, wherein the phenyl of the anilino group is substituted with a 4-trifluoroacetamido group. The instant claim differs by having the $\text{-NH-C(O)-(CH}_2\text{)}_q\text{-R}^4$ substituent which is structurally analogous to the trifluoroacetamido of the reference compound, at the 3-position as compared to the 4-position in the reference. It is well established in the art

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that positional isomerism involves ‘close structural similarity’. Compounds which are positional isomers (compounds having the same radicals in physically different positions on the same nucleus) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

Applicant cites *In re Jones* to overcome the obviousness rejection. However, *Jones* dealt with the obviousness of a particular claimed ammonium salt based on a generic teaching of “substituted ammonium salts” with no Markush recitation for particular moiety, aminoethoxy ethanol, the salt on appeal. Secondary references applied in *Jones* were deemed not properly combinable with the generic disclosure in the primary reference since the references were not all from the same art area. Unlike the situation in *Jones*, the instantly claimed compounds are obvious structural variants of compounds expressly taught by the reference. As explained above, the reference generically discloses all the elements of the instantly claimed genus and further, provides an example that differs only by the position of the substituent. Thus, the reference provides sufficient motivation for the ordinary artisan to modify the reference compounds to arrive at the instantly claimed compounds because one of ordinary skill in the art only needs to change the position of the substituent to arrive at the instant invention. Such modification would have been obvious, absent a showing of unexpected results.

Applicant cites *In re Baird* and argues that the genus of the reference is not sufficient to establish a *prima facie* case of obviousness. This is not found to be persuasive because the

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decision in *Baird* was based on a big genus encompassing millions of compounds vs. a small number of claimed species, “[A] disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds.” 29 USPQ2d 1552. However, the instant case involves a genus vs. genus and not a broad genus vs. a small number of species. More specifically, the reference clearly teaches bicyclic pyrimidine compounds having a 4-anilino substituent and further discloses specific example (see compound #129) and thus, the instantly claimed compounds are clearly suggested by the reference. Therefore, motivation exists to modify the prior art genus to prepare the instantly claimed compounds with the reasonable expectation of obtaining compounds having similar properties.

Applicant further argues that the preferred substitution in the reference is at the para position and the most preferred substituent is halogen (e.g. fluorine) and therefore, the reference does not motivate the person of ordinary skill in the art to prepare instantly claimed compounds wherein the amido group is at the 3-position of the phenyl ring. However, the reference discloses compounds wherein the phenyl is substituted at the 3-position also, and therefore, provides suggestion to one of ordinary skill in the art. “Structural relationships provide the requisite motivation or suggestion to modify known compounds to obtain new compounds.” See *In re Duel*, 51 F.3d at 1558, 34 USPQ2d at 1214. Reference must be considered, under 35 U.S.C. 103, not only for what it expressly teaches but also for what it fairly suggests; all disclosures of prior

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art, including unpreferred embodiments, must be considered in determining obviousness. *In re Burckel*, 201 USPQ 67 (CCPA 1979).

For all the above reasons the rejection is maintained.

3. Claims 1, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiesenfeldt et al., EP 447891, for the reasons provided in the previous office action which are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that the reference teaches away from the instantly claimed invention because the reference does not teach a single compound which falls within the scope of the present claims. The reference, however, clearly teaches a bicyclic pyrimidinyl core (see the formula disclosed in Table 1, page 13) and further teaches several examples having a 4-anilino group (see compounds 217-266) including a species wherein the phenyl of the anilino group is substituted with 4-NH-CO-CH₃ (i.e., compound no. 249). It is to be noted that rejection under 35 U.S.C. 103 is proper where the subject matter claimed "is not *identically* disclosed or described" in the prior art, and the prior art directs those skilled in the art to the compounds, without any need for picking, choosing, and combining various disclosures. See *In re Shaumann et al.*, 572 F.2d 312, 315, 316, 197 USPQ 5, 8, (CCPA 1978). In the instant case, the reference teaches a smaller genus than that of the instant claims and further, discloses a specific compound that differs only by the position of a single substituent and thus, provides motivation to one of ordinary skill in the art to prepare other useful compounds. "The question under 35 U.S.C. 103

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is not merely what the reference expressly teaches but what it would have suggested to one of ordinary skill in the art at the time the invention was made.” (Rebuttal reasons provided for the Ugarkar reference are also included here).

For all the above reasons the rejection is maintained.

Allowable Subject Matter

Claims 2-8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

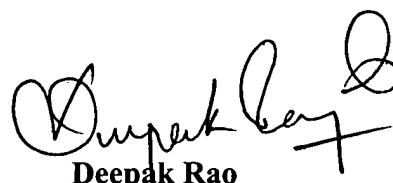
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will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (703) 305-1879. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (703) 308-4716. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


Deepak Rao
Primary Examiner
Art Unit 1624

September 23, 2003